GCCAGGTCTGGCACCATGCACTAGGATACCCAGAACGCTGCAAGGCCACGCC CTCCTCACTTCAGGGGTCACTCTCCCCATTGCCCACCACCACCACCATGGCTGGG GATCGGCTCCCGAGGAAGGTGATGGACGCAAAGAAACTGGCCAGCCTGCTGC GTGGCGGCCTGGGGACCCTTGGTCATCGACAGCCGGTCCTTCGTGGAGTAT AACAGCTGCCACGTGCTGAGCTCTGTGAATATCTGCTGTTCAAAGCTGGTGAA GCGGCGCCTTCAGCAGGGAAAAGTGACAATTGCTGAGCTTATCCAGCCTGCTA CACGGAGCCAGGATGCCACAGAACCACAGGATGTAGTGGTGTATGACCA GAGCACACGAGATGCCAGCGTGCTGGCAGCAGACAGCTTCCTGTCCATCCTGC TCAGCAAGCTGGACGGCTTCGACAGTGTGGCCATCCTCACAGGAGGCTTC GCCACCTTCTCCTGCTTCCCTGGCCTCTGTGAGGGCAAGCCTGCCACTCTA CCGTCCATGAGCCTCTCAGCCCTGCCTGCCTGTGCCCAGTGTTGGCCTGACC CGAATCCTGCCTCACCTCTACCTGGGCTCTCAGAAAGATGTCTTGAACAAGGA TCTGATGACCCAAAACGGAATAAGCTATGTCCTCAATGCCAGCAACTCCTGCC CTAAACCGGACTTCATCTGTGAGAGCCGTTTCATGCGTATCCCCATCAATGAC AACTACTGTGAAAAGCTGCCCTGGCCTGGACAAGTCCATCGAGTTTATTGA TCGCTCTGCCACCATTGCCATCGCGTACATCATGAAAACCATGGGCATGTCTTC TGACGACGCATACAGGTTTGTGAAGGATCGGCGCCCCTCCATCTCGCCCAACT TCAACTTCCTGGGCCAGTTGCTGGAGTATGAGAGGAGTCTGAAGCTGCTGGCT GCCCTGCAGACTGATGGACCTCACTTGGGGACCCCTGAGCCCCTCATGGGCCC GGCAGCAGCATCCCACTGCCCCGGCTGCCACCATCTACCTCAGAGAGCGCTG CCACTGGGAGCGAGCCACCGCAGCCAGGGAGGGCAGCCCAAGTGCTGG AGGGGATGCTCCGATCCCCAGCACAGCTCCAGCCACCAGCGCGCTGCAGCAG GGCCTGCGTGCCCTCCTCTCTCTGACCGCCTCCAGGACACCAACCGCCT CAAGCGTTCCTTTTCCCTGGACATCAAGTCGGCCTATGCACCCAGCAGGAGGC CCGACTTTCCCGGCCCACCCGACCCCGGTGAAGCCCCGAAGCTCTGCAAGCTG GACAGCCCGTCTGGGGCACACTGGGCCTGCCCTCGCCCAGCCCAGACAGCCC GGACTCCGTTCCAGAGTGCCGCCCACGACCCCGGCGACGCCCCCCGGCTA GTTCGCCTGCCCCCCCCCCCCCATGGTCTGGGCCTGAACTTTGGAGACACG GCCCGGCAGACTCCACGGCACGGCCTCTCGGCCCTGTCGGCGCCCCGGGCTGCC TGGCCCTGGCCAGCCGGCTGGCCCCGGGGGGCTGGCCGCCACTGGACTCCC CAGGCACACCGTCGCCCGACGCCCCTGGTGCTTCAGCCCCGAGGGCGCGCA GGGTCCAGGCGCTGTGTTCTCCGCCTTTGGCCGGGTAAGTGCAGGCGCACCTG GACCCGGTAACAGCAGCAGCAGCGGTGGTGGTGGTGGTGGTGGCGCGG CAGCAGCAGCAGCAGCAGCAGCAGTAGTAGTAGTAGTGACCTG CGGAGGCGGATGTGCGGACCGGCTGGCCCGAGGAGCCTGCTGCAGATGCAC AGTTCAAGAGGCGCAGCTGCCAGATGGAGTTCGAAGAGGGCATGGTGGAGGG GCGGGCACGTGGCAGCTGGCAGCCTGGGCAAGCAAACCAGCTTCTCT GGCAGCGTGGAGGTCATCGAAGTATCGTGACCCTTCAGAAGTCCCTGTGCCCT TGCTCCAGCCAGGCCAGGTATAAATATATATATATATAAAAACACACAGAAAA GGTAAATGGTTTTACTGCAATTTTTATCAAGAAGTAAATATTTCGATTTTTAT TTATTTAAGCTAGTGATCTGGCAACTGTGCGGGGGGGCGCCCTAAAGCTCTGTTTT TACTGTCTGGTATTTAAACTGAAACAGGTTTCTAAGCAATATGAGGCCACCTT CAATCCCAAACTGGGTTGACAGGCCTGGGCCCCTCCTTGCCCCTCTCGG AAACATTACTGACCTTTCAAAGAGCTGCCCAGCTTTCCTGCACTTTTTACATAA GAAAAAGGGGGGGGGGAA (SEQ ID NO:1)

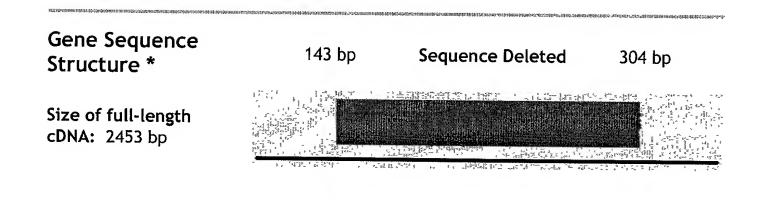
FIGURE 1

<u>underlined</u> = deleted in targeting construct

[] = sequence flanking Neo insert in targeting construct

[GCCAGGTCTGGCACCATGCACTAGGATACCCAGAACGCTGCAAGGCCACGCCCTCCTCAC TTCAGGGGTCACTCTCCCCATTGCCCACCACCACCATGGCTGGGGATCGGCTCCCGAG GAAGGTGATGGACGCAAAGAAA] CTGGCCAGCCTGCTGCGTGGCGGGCCTGGGGGGACCCTT $\hbox{\tt GGTCATCGACAGCCGGTCCTTCG} \overline{\hbox{\tt TGGAGTATAACAGCTGCCACGTGCTGAGCTCTGTGAA}}$ TATCTGCTGTTCAAAGCTGGTGAAGCGGCGCCTTCAGCAGGGAAAAGTGACAATTGCTGA GCTT[ATCCAGCCTGCTACACGGAGCCAG]GTGGATGCCACAGAACCACAGGATGTAGTGGT GTATGACCAGAGCACACGAGATGCCAGCGTGCTGGCAGCAGACAGCTTCCTGTCCATCCT GCTCAGCAAGCTGGACGGCTTCCGACAGTGTGGCCATCCTCACAGGAGGCTTCGCCAC $\verb|CTTCTCCTGCTTCCTGGGCCTCTGTGAGGGCAAGCCTGCCACTCTACCGTCCATGAG| \\$ $\tt CCTCTCTCAGCCCTGCCTGTGCCCAGTGTTGGCCTGACCCGAATCCTGCCTCACCT$ CTACCTGGGCTCTCAGAAAGATGTCTTGAACAAGGATCTGATGACCCAAAACGGAATAAG $\tt CTATGTCCTCAATGCCAGCAACTCCTGCCCTAAACCGGACTTCATCTGTGAGAGCCGTTT$ CATCGAGTTTATTGATAAAGCCAAGCTGTCCAGCTGCCAAGTCATTGTTCACTGTCTGGC TGGCATCTCTCGCCTCTGCCACCATTGCCATCGCGTACATCATGAAAACCATGGGCATGTC TTCTGACGACGCATACAGGTTTGTGAAGGATCGGCGCCCCTCCATCTCGCCCAACTTCAA TGATGGACCTCACTTGGGGACCCCTGAGCCCCTCATGGGCCCGGCAGCAGCATCCCACT GCCCCGGCTGCCACCATCTACCTCAGAGAGCGCTGCCACTGGGAGCGAGGCAGCCACCGC AGCCAGGGGGGGCCCCAAGTGCTGGAGGGGGATGCTCCGATCCCCAGCACAGCTCCAGC CACCAGCGCGCTGCAGGGCCTGCGTGGCCTCCTCTCTCTGACCGCCTCCAGGA CACCAACCGCCTCAAGCGTTCCTTTTCCCTGGACATCAAGTCGGCCTATGCACCCAGCAG GAGGCCCGACTTTCCCGGCCCACCCGACCCCGGTGAAGCCCCGAAGCTCTGCAAGCTGGA CAGCCCGTCTGGGGCACACTGGGCCTGCCCTCGCCCAGACAGCCCGGACTCCGT TCCAGAGTGCCGCCCACGACCCCGGCGACGCCCCCGGCTAGTTCGCCTGCCCGCTC CCCCGCGCATGGTCTGGGGCCTGAACTTTGGAGACACGGCCCGGCAGACTCCACGGCACGG CCTCTCGGCCCTGTCGGCCCCGGGCTGCCTGGCCAGCCGGCTGGCCCCGGGGG CTGGGTGCCGCCACTGGACTCCCCAGGCACACCGTCGCCCGACGCCCCTGGTGCTTCAG CCCCGAGGGCGCGCAGGGTCCAGGCGCTGTGTTCTCCGCCTTTTGGCCGGGTAAGTGCAGG CAGCAGCAGCAGCAGCAGTAGTAGTAGTAGTAGTGACCTGCGGAGGCGGGATGTGCG GACCGGCTGGCCGAGGAGCCTGCTGCAGATGCACAGTTCAAGAGGCGCAGCTGCCAGAT GGAGTTCGAAGAGGGCATGGTGGAGGGGGGGGGGCACGTGGCAGGCGTGGCAGCCCTGGG CAAGCAAACCAGCTTCTCTGGCAGCGTGGAGGTCATCGAAGTATCGTGACCCTTCAGAAG GAAAAGGTAAATGGTTTTACTGCAATTTTTTATCAAGAAGTAAATATTTCGATTTTTATT TATTTAAGCTAGTGATCTGGCAACTGTGCGGGGGGCGCCCTAAAGCTCTGTTTTTACTGTC TGGTATTTAAACTGAAACAGGTTTCTAAGCAATATGAGGCCACCTTCAATCCCAAACTGG GTTGACAGGCCTGGGCCCCTCTTGCCCCTCTCGGAAACATTACTGACCTTTCAAA

FIGURE 2A

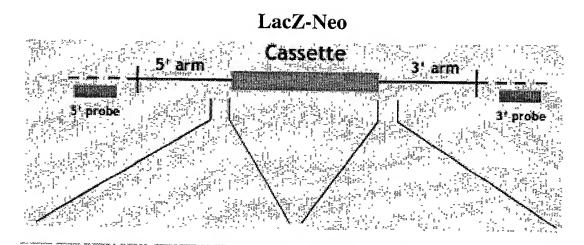


Targeting Vector* (genomic sequence)

Arm Length: 5': 2.5 kb 3': 2 kb

Targeting Vector

* Not drawn to scale



(SEQ ID NO:2)

5'>ATCCAGCCTGCTACACGAAGC CAGGTACCTGTGGCCCACCCTTGC ATGCGTCTTCAGGGCTGACCATTC CTGAGCAAACAGACCTATGTCACC TCTGAAAGAGACAGAGGAGCTCCC AGGCCTGGTGCCAAGAGTCCTCTG ATAAGGCATTTCCCCCTCGCTGTC CCTCCGTTCCAAACAGGGTTCCTT GGGGTCAGAGC<3' (SEQ ID NO:3)

FIGURE 2B